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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,217	06/05/2000	EMMANUELLE GUILLOT	1029/00196	1395

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EXAMINER

SOUAYA, JEHANNE E

ART UNIT PAPER NUMBER

1634

DATE MAILED: 08/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/529,217	Applicant(s) GUILLOT ET AL.	
	Examiner Jehanne E Souaya	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 08 January 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

1. Currently, claims 1-30 are pending in the instant application. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following rejections are either newly applied or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Maintained Rejections

Claim Rejections - 35 USC § 112

3. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps or elements, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are as follows. Claim 1 recites "extracting the hybridized specific probes from their target by adding a denaturing agent to denature the probe target complex...", however the step fails to indicate what the denaturing agent is being added *to*. For example, the denaturing agent could be added to the solution that contains the microorganisms that contain the probe-target complex, which the specification teaches is the invention and which is indicated in applicants responses, or the denaturing agent could be added to a solution containing only the probe-target complex which was extracted from the whole cells. Applicants' responses, however, indicate that the former scenario is the invention, for example, the response

of 12/6/2001 states at page 6 (end of last full para), "claim 1 was amended to better define the extraction and separation of the hybridized probes *from the cells* for quantitative detection".

Response to Arguments

The response indicates that the claims have been amended to address the 112/2nd paragraph issues raised in paragraph 5 from the previous office action. However, the amendment to claim 1 is not sufficient to overcome the rejection because the claims still encompass extraction of the probe from the target and measurement within the cell. That is, the claims are not limited to extracting the probes *from the cells*.

4. Claims 20-23, 25, and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

C) Claims 20-23 are indefinite in that it is unclear what the term "it" in line 1 of each claim refers to. If the term is meant to refer to the method, the claim should be amended to reflect such, for example: "the method according to claim 1, wherein said method is used ...".

D) Claim 25 lacks sufficient antecedent basis for the recitation of "said denaturing agent concentration", said Tris HCl concentration" and "said salt concentration". This rejection can be overcome by reciting instead for example" the concentration of said denaturing agent".

E) Claim 25 is indefinite as it is unclear what range of concentrations is encompassed by the terminology of "on the order of". The specification does not define this recitation, and therefore, the metes and bounds of the claim are unclear.

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F) Claim 29 lacks sufficient antecedent basis for the recitation of "said fixation solution".

Response to Arguments

These rejections have not been addressed either by arguments or by amendment in the previous response.

Claim Rejections - 35 USC § 103

5. Claims 1-12, 16-18, and 24-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mayrand (US Patent 5,691,146, 102(e) date: 5/5/1995), in view of Burton, Journal of Experimental Marine Biology and Ecology, 1996, vol. 200, abstract, p. 85), and Nuovo et al (US Patent 5,538,871, 7/23/1996) and further in view of De Los Reyes, and Mobarry.

Mayrand teaches that in situ hybridization and amplification can be performed using primers and fluorescently labeled probes (see cols 4 and 5). (see US Patent 5,538,871 for in situ PCR conditions, reference provided). Burton teaches that bacteria can be detected by in situ PCR. De Los Reyes and Mobarry teach universal and specific probes for the detection of microbial populations in waste water. Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the application was made to use the method of Mayrand under in situ PCR conditions for the detection of microbial populations as Burton teaches that in situ PCR can be used to detect bacteria and De Los Reyes and Mobarry teach probes useful for detecting microbial populations under in situ conditions. The ordinary artisan would have been motivated to use the method of Mayrand, that is to include probes in *in situ* PCR because Mayrand teaches that the method of contacting a target nucleic acid with PCR reagents and

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specific probes allows a the amplification and detection of target nucleic acid in a single reaction vessel using a single reagent. Although the instantly claimed invention does not specify in situ PCR, the instantly claimed invention is drawn to a method comprising and does not exclude in situ PCR. Further, the method of Mayrand teaches contacting target with PCR reagents and a probe, and during the subsequent thermal cycling steps, the probe of Mayrand will dissociate from the target. Thus the temperature change can be an agent that brings about dissociation or denaturation of the probe from the target. It is noted that Mayrand does not teach elution or detection of the probe outside the cell, however the presently claimed invention is not drawn to such.

Response to Arguments

The response traverses the rejection. The response asserts that the Mayrand and Burton references disclose methods of in situ PCR, which does not allow for the quantification of DNA in the original sample. This argument has been thoroughly reviewed but was found unpersuasive because the claims are not limited to quantification of DNA in the original sample. While the preamble states a method of qualitative and quantitative analysis of microbial populations, the final step achieves such by detecting extracted probes from a probe target complex. Given the broadly recited “comprising” language in the claims, the claims are not limited to quantifying DNA in the original sample. Further, regardless of such, the claim does not make clear how the method “quantitatively” analyzes microorganisms in a sample. The recitation of “quantitative analysis” is not limited to “quantification of DNA in the original sample” or quantification of the number of microorganisms in a sample. As Mayrand specifically teaches measurement of fluorescence emissions, such is considered “quantitative analysis” as recited in the claims.

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The response further asserts that applicants' inventive process is completely different than the PCR process described in Mayrand and Burton. The response asserts that the instant method targets RNA and not DNA. This argument has been thoroughly reviewed but was found unpersuasive as the method of Mayrand could be used to target either RNA or DNA as exemplified by the specific teaching in Mayrand that dUTP could be used (see col. 4, line 60). The response also asserts that the RNA sample in the instant claims is not amplified by a thermal enzyme process and instead the claimed process is directed to the extraction and quantification of the probe after in situ hybridization. This argument has been thoroughly reviewed but was found unpersuasive as the instant claims do not preclude PCR. As the instant claims are drawn to a method "comprising" steps, the instant claims do not rule out PCR. Further, the claims do not limit the extraction and quantification of probes after in situ hybridization. This feature upon which applicant relies is not recited in the rejected claim(s). In other words, the claims are not limited to extraction of the probes outside of the whole cells. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Conclusion

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO**

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. No claims are allowable.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703) 308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Jehanne Souaya
Primary Examiner
Art Unit 1634

July 29, 2003